Patent US 2000-043

Attorney Docket: 612,406-043

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims

1-10. (Cancelled)

11. (New) A method for the detection of the malignancy of melanoma cells in a patient sample, comprising the steps of:

providing a patient sample containing a BRAF sequence containing codon 599 of exon 15;

providing a first oligonucleotide probe comprising a first label, wherein the oligonucleotide probe is complementary to a wildtype BRAF sequence containing codon 599;

providing a second oligonucleotide probe comprising a second label, wherein the second oligonucleotide probe is complementary to a mutant BRAF sequence containing a mutation at codon 599;

contacting the patient sample with the first and second oligonucleotide probes to hybridize at least one of the fist and second oligonucleotide probes with the patient sample; and detecting the at least one of the fist and second oligonucleotide probes hybridized with the patient sample.

12. (New) The method of claim 11, wherein the first oligonucleotide probe comprises a sequence selected from the group consisting of Seq. ID No. 5, a sequence complementary to Seq. ID No. 5, a sequence substantially homologous to Seq. ID No. 5, and a sequence complementary to a sequence substantially homologous to Seq. ID No. 5.

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- 13. (New) The method of claim 11, wherein the first oligonucleotide probe comprises a sequence selected from the group consisting of **Seq. ID No. 1**, a sequence complementary to **Seq. ID No. 1**, and a sequence complementary to a sequence substantially homologous to **Seq. ID No. 1**.
- 14. (New) The method of claim 11, wherein the second oligonucleotide probe comprises a sequence selected from the group consisting of Seq. ID No. 6, a sequence complementary to Seq. ID No. 6, a sequence substantially homologous to Seq. ID No. 6, and a sequence complementary to a sequence substantially homologous to Seq. ID No. 6.
 - 15. (New) The method of claim 11, wherein codon 599 codes for valine.
- 16. (New) The method of claim 15, wherein codon 599 is selected from the group consisting of GTG, GTA, GTC, and GTT.
- 17. (New) The method of claim 11, wherein codon 599 that contains the mutation codes for an amino acid selected from the group consisting of glutamic acid and aspartic acid.
- 18. (New) The method of claim 17, wherein codon 599 that contains the mutation is selected from the group consisting of GAG, GAA, GGG, GGA, GGC, and GGT.
- 19. (New) A method for the detection of the malignancy of melanoma cells in a patient, comprising the steps of:

providing a patient sample containing a BRAF sequence containing codon 599 of exon 15;

sequencing the patient sample; and determining the presence of a mutation at codon 599 of exon 15.

- 20. The method of claim 19, wherein codon 599 that contains the mutation codes for a glutamic acid or an aspartic acid.
- 21. The method of claim 19, further comprising the step of amplifying the patient sample before sequencing the patient sample.

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22. (New) A method for the detection of the malignancy of melanoma cells, comprising the steps of:

providing an oligonucleotide probe selected from the group consisting of exon 15 of the BRAF gene, a part of exon 15 of the BRAF gene comprising codon 599, and the counterstrands thereto;

hybridizing the oligonucleotide probe with a wildtype reporter comprising a sequence according to **Seq. ID No. 5** and a first label;

hybridizing the oligonucleotide probe with a mutant reporter comprising a second label, wherein the mutant reporter is selected from the group consisting of a sequence according to Seq. ID No. 6, a sequence complementary to Seq. ID No. 5, a sequence complementary to Seq. ID No. 6, a sequence with a homology of over 80% to Seq. ID No. 6, a sequence with a homology of over 80% to a sequence complementary to Seq. ID No. 5, and a sequence with a homology of over 80% to a sequence complementary to Seq. ID No. 6; and

detecting a signal from the first label and a signal from the second label.

- 23. (New) The method of claim 22, further comprising the step of determining a ratio of the signal from the first label and the signal from the second label.
- 24. (New) The method of claim 22, wherein the oligonucleotide probe is a part of exon 15 of the BRAF gene.
- 25. (New) The method of claim 24, wherein the part of exon 15 of the BRAF gene is selected from the group consisting of Seq. ID No. 1, an oligonucleotide comprising a sequence complementary to Seq. ID No. 1, a part of Seq. ID No. 1 comprising codon 599, and an allelic variant of Seq. ID No. 1.
- 26. (New) The method of claim 22, wherein the oligonucleotide probe comprises codon 599, wherein codon 599 codes for Valine (Val, V).
- 27. (New) The method of claim 22, wherein the oligonucleotide probe comprises a mutation at codon 599.

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28. (New) The method of claim 27, wherein the mutation codes for a glutamic acid (Glu, E) or an aspartic acid (Asp, D).

29. (New) The method of claim 22, further comprising the step of detecting a mutation in codon 599 of the oligonucleotide probe.